

REMARKS

Applicants respectfully request the Examiner to reconsider the merits of the objections and rejections in view of the foregoing amendment and following remarks.

Upon entry of the foregoing amendment, claims 1, 3, 6-14, 16-19 and 21-23 are pending in the Application. Claims 1, 3, 6, 8-14, 16, 17 and 21-23 are amended. Claims 2, 4, 5, 15, 20 and 24-27 are canceled.

Applicants respectfully request entry of the above amendment and submit that the above amendment does not constitute new matter.

Applicants have amended claims 1, 3, 6, 8-14, 16, 17 and 21-23 for the sole purpose of expediting prosecution by enhancing readability in the context of the subject matter. Support for the amendments to these claims can be found throughout the Specification and in the claims as originally filed. In particular, support for the amendment to claim 1 can be found, *inter alia*, in the Specification at page 5, para. [021], lines 4-7; page 10, para. [052], lines 3-6; page 9, para. [048], lines 4-13; page 8, para. [47], line 33 to page 9, para. [47], line 3; page 10, para. [55], lines 27-29.

Based on the instant amendment and remarks, Applicants respectfully request that the Examiner withdraw the outstanding objections and rejections.

I. Sequence Compliance

Applicants appreciate the Examiner pointing out the portions of the specification in which Sequence Identification Numbers were inadvertently omitted. The instant Amendment to the Specification includes an amendment incorporating the sequence identification numbers corresponding to the nucleotide sequences in accordance with Applicants' previously-submitted Submission of Sequence Listing filed June 1, 2004. Therefore, Applicants believe that they have addressed the sequence listing compliance issue raised by the Examiner and that the instant Reply brings the Application into full compliance with 37 C.F.R. §§ 1.821-1.824.

II. Objection to Specification

The Examiner pointed out certain typographical and grammatical errors in the Specification that the Examiner stated should be amended and also pointed out some stylistic

changes that the Examiner stated should be incorporated into the Specification. Set forth in the instant Reply are Amendments to the Specification which include the Examiner's suggested changes. In view of the Amendments to the Specification, Applicants request the Examiner to withdraw the objections to the Specification.

III. Objection to Claim

The Office Action stated that claim 14 is objected to because it contained a typographical error in reciting "conibination." Applicants thank the Examiner for pointing out this typographical error and have included a correction to this error in amended claim 14, rendering the objection to claim 14 moot.

IV. Rejection under 35 U.S.C. § 112, para. 2

The Office Action stated that claims 1-24 are rejected under 35 U.S.C. § 112, para. 2, as allegedly being indefinite. (Office Action, page 4.) Applicants respectfully disagree. However, to expedite prosecution and enhance readability, Applicants amended claims 1, 3, 6, 8-14, 16, 17 and 21-23. Also to expedite prosecution, claims 2, 4, 5, 15, 20 and 24-27 are canceled. Therefore, the rejection of claims 2, 4, 5, 15, 20, 24-27 under § 112, para. 2, has been rendered moot.

Furthermore, Applicants respectfully submit that amended claims 1, 3, 6, 8-14, 16, 17 and 21-23 and claims 7, 18 and 19 are clearly definite. Applicants note that claim 1, as amended, does not contain the language in previous claim 1 which the Examiner pointed out in making the rejection based on indefiniteness, i.e., "heteroduplex polynucleotide comprises at least one annealed fragment," "homologous heteroduplex," "one homologous heteroduplex," "until," "said" before "fragment," "preparing" in the preamble and "exposing at least one homologous heteroduplex." One of skill in the art would clearly understand the metes and bounds of claim 1, as amended. Indeed, a method involving obtaining polynucleotide fragments by obtaining a library of homologous polynucleotides by mutagenesis, denaturing and hybridizing said polynucleotides to form heteroduplex polynucleotides, cleaving said heteroduplex polynucleotides by using proteins of a polynucleotide repair system and denaturing said cleaved heteroduplex polynucleotides to obtain fragments, clearly and precisely delineates the scope of Applicants' inventive subject matter to the skilled artisan.

Furthermore, amended claims 11-13 do not contain the phraseology in previous claims 11-13 which the Examiner mentioned in making the rejection based on indefiniteness, i.e., “complex” and “combination thereof.” Amended claims 11-13 clearly convey the subject matter of polynucleotide repair system enzymes “or a combination of enzymes thereof,” which the Examiner stated would be remedial. (Office Action, pages 6-7.)

Applicants also point out that amended claims 14 and 22-23 contain sufficient antecedent support in claim 1, as amended.

Consequently, at least in view of the above remarks, Applicants respectfully assert that claims 1, 3, 6-14, 16-19 and 21-23 are clearly definite, and requests the Examiner to withdraw the rejection of claims 1, 3, 6-14, 16-19 and 21-23 under § 112, para. 2.

V. Rejection under 35 U.S.C. § 102(e)

The Office Action stated that claims 1-13, 15-18 and 20-27 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,537,746 issued to Arnold, et al. (the “Arnold ’746 patent”), which was filed on December 4, 1998. Applicants respectfully traverse this rejection of claims 1-13, 15-18 and 20-27 both as originally filed and as amended. However, claims 2, 4, 5, 15, 20 and 24-27 have been canceled to expedite prosecution, and thus the rejection with respect to these claims has been rendered moot. Regarding the rejection of claims 1, 3, 6-13, 16-18 and 21-23, Applicants respectfully traverse.

Applicants’ invention is directed to a method for obtaining polynucleotide fragments. Applicants’ independent claim 1 encompasses the invention of: obtaining a library of homologous polynucleotides from a parental polynucleotide by mutagenesis, denaturing and hybridizing said polynucleotides to form heteroduplex polynucleotides, cleaving said heteroduplex polynucleotides by using proteins of a polynucleotide repair system which cleave mismatched base pairs, and denaturing said cleaved heteroduplex polynucleotides to obtain fragments.

By distinct contrast, the Arnold ’746 patent discloses “methods for evolving a polynucleotide.” (Arnold ’746 patent, Abstract.) This is *not* a method for obtaining polynucleotide fragments. Rather, the Arnold ’746 patent discloses:

Annealing can . . . form heteroduplexes The products of annealing are exposed to enzymes of a DNA repair, and optionally a replication system, that repairs unmatched pairings. . . . Exposure

of heteroduplexes to a DNA repair system results in DNA repair
. . . in the heteroduplexes

(Arnold '746 patent, col. 7, ll.1-12.)

According the Arnold '746 patent, the heteroduplexes are exposed to a cellular DNA repair system to convert the heteroduplexes to parental polynucleotide variants or recombined polynucleotide variants. (Arnold '746 patent, Abstract.)

Applicants' invention, therefore, which involves *cleaving* heteroduplex polynucleotides and *denaturing the cleaved polynucleotides* is not anticipated by the Arnold '746 patent. The Arnold '746 patent does not disclose obtaining polynucleotide fragments by denaturing cleaved heteroduplex polynucleotides. Nowhere in the Arnold '746 patent is it disclosed that a heteroduplex polynucleotide is cleaved by proteins of a polynucleotide repair system which can cleave mismatched base pairs and that a cleaved heteroduplex is denatured to obtain fragments.

The portions of the Arnold '746 patent cited by the Examiner do not disclose obtaining polynucleotide fragments by denaturing cleaved heteroduplex polynucleotides. In particular, the Office Action cited col. 2, ll. 40-45 and claim 7 of the Arnold '746 patent to support the contention that "[t]he heteroduplexes are exposed to repair system so as to convert the heteroduplexes to parental polynucleotide variants (i.e. fragments)." (Office Action, page 9). However, the cited text of the Arnold '746 patent does *not* disclose that "parental polynucleotide variants" are "fragments," and there is nothing in the Arnold '746 patent that teaches that "parental polynucleotide variants" are fragments obtained by the method involved in Applicants' invention.

The Office Action stated that "heteroduplexes are denatured into single-stranded molecules that are subsequently re-annealed" and cites col. 2, ll. 60-67; col. 3, ll. 20-30; col. 8, l. 65; and claims 1 and 9 to support this statement. However, these cited portions of the Arnold '746 patent do *not* teach denaturing of heteroduplexes. For example, the text at col. 2, ll. 60-67 of the Arnold '746 patent discloses "[t]he first and second vectors are converted to linearized forms," and then, according to the Arnold '746 patent, the linearized forms anneal to form a heteroduplex. (Arnold '746 patent, col. 2, l. 63 to col. 3, l. 2.) This is not denaturing a heteroduplex. Nor do the other cited portions of the Arnold '746 patent disclose denaturing of heteroduplexes.

In sum, then, none of the Examiner-cited portions of the Arnold '746 patent nor any other portion of the Arnold '746 patent discloses obtaining polynucleotide fragments by cleaving heteroduplex polynucleotides with proteins which can cleave mismatched base pairs and denaturing the cleaved heteroduplex polynucleotides to obtain fragments, which are features of independent claim 1. The remaining pending claims depend directly or indirectly from claim 1. Accordingly, Applicants respectfully request the Examiner to withdraw the rejection of claims 1-13, 15-18 and 20-27 under § 102(e) and permit claims 1, 3, 6-14, 16-19 and 21-23 to pass to allowance.

CONCLUSION

Applicants respectfully request entry of the above claim amendments.

All of the stated grounds of objection and rejection have been properly traversed, accommodated or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

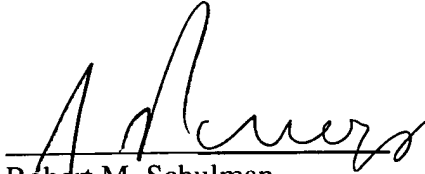
The Examiner is respectfully requested to contact the undersigned by telephone at the below listed telephone number, in order to expedite resolution of any issues and to expedite passage of the present application to issue, if any comments, questions, or suggestions arise in connection with the present application.

In view of the above claim amendments and remarks, early notification of a favorable consideration is respectfully requested. The instant Reply is being submitted concurrently with a Petition for One-Month Extension of Time and a check in the amount of \$60.00 (small entity). The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account Number 50-0206.

Respectfully submitted,

Dated: 3/3/06

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